

What is claimed is:

1. A method for the treatment of Type 2 diabetes mellitus and conditions associated with diabetes mellitus, which method comprises the administration to a human or non-human mammal in need thereof, of an effective non-toxic amount of an insulin sensitiser so as to provide a plasma concentration of the insulin sensitiser of at least a threshold level (the Threshold Plasma Concentration) from within the range of effective plasma levels of the insulin sensitiser.
- 10 2. A method according to claim 1, wherein the Threshold Plasma Concentration is within the range of from about 40 to about 200ng/nL.
- 15 3. A method according to claim 1 or claim 2, wherein the Threshold Plasma Concentration is within the range of from about 50 to about 120ng/mL or about 60 to about 120ng/mL or about 90 to about 110ng/mL or about 95 to about 105ng/mL.
- 20 4. A method according to any one of claims 1 to 3, wherein a minimum value of the Threshold Plasma Concentration (or the Minimum Threshold Plasma Concentration) of the insulin sensitiser is its SC50 concentration.
- 25 5. A method according to any one of claim 1 to 4, wherein a Preferred Threshold Plasma Concentration for the insulin sensitiser is twice the SC50 concentration.
- 30 6. A method according to any one of claim 1 to 5, wherein the plasma concentration of the insulin sensitiser remains substantially within the range from the Minimum Threshold Plasma Concentration to a level at or above the Preferred Threshold Plasma Concentration.
7. A method according to any one of claim 1 to 6, wherein the insulin sensitiser is Compound (I).
- 35 8. A method according to any one of claims 4 to 6, wherein the insulin sensitiser is Compound (I) and the SC50 is within the range of 40 to 65 ng/mL.

9. A method according to claim 8, wherein the SC50 of Compound (I) is 51.4ng/mL.

10. A method according to any one of claims 6 to 9 wherein the insulin sensitiser is Compound (I) and the Preferred Threshold Plasma Concentration is in the range of about 80 to about 130 ng/mL or about 82.2 to about 123.4.

11. A method according to claim 10, wherein the Preferred Threshold Plasma Concentration for Compound (I) is 100 ng/mL or 102.8 ng/mL.

12. A method according to claim 1, wherein the insulin sensitiser is Compound (I) and its plasma concentration remains substantially within the range of from 40 ng/mL to at or above 130 ng/mL or 41.1 ng/mL to at or above 123.4 ng/mL, for example 50ng/mL to at or above 100ng/mL or 51.4ng/mL to at or above 102.8ng/mL.

13. A method according to claim 10, wherein the insulin sensitiser is Compound (I) and its plasma concentration remains substantially at or above its Preferred Threshold Plasma Concentration.

14. A method according to claim 13, wherein the insulin sensitiser is Compound (I) and its plasma concentration remains at or above 100ng/mL or substantially at or above 102.8ng/mL.

15. A method according to any one of claims 1 to 6, wherein the insulin sensitiser is 5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]-2,4-thiazolidinedione (or troglitazone), 5-[4-[(1-methylcyclohexyl)methoxy]benzyl] thiazolidine-2,4-dione (or cigitazone), 5-[4-[2-(5-ethylpyridin-2-yl)ethoxy]benzyl] thiazolidine-2,4-dione (or pioglitazone) or 5-[(2-benzyl-2,3-dihydrobenzopyran)-5-ylmethyl]thiazolidine-2,4-dione (or englitazone).

16. A pharmaceutical composition comprising an insulin sensitiser and a pharmaceutically acceptable carrier therefor, which composition is adapted to provide a plasma concentration of the insulin sensitiser of at least a Threshold Plasma Concentration of the insulin sensitiser.

17. A pharmaceutical composition according to claim 17 wherein the composition is adapted to provide a plasma concentration of the insulin sensitiser of at least a Threshold Plasma Concentration over a sustained period of time.

5 18. A modified release pharmaceutical composition comprising an insulin sensitiser and a pharmaceutically acceptable carrier therefor, which composition is adapted to provide a plasma concentration of the insulin sensitiser of at least a Threshold Plasma Concentration of the insulin sensitiser.

10 19. A modified release composition according to claim 1 being a delayed, pulsed or sustained release composition.

20. A composition according to any one of claim 16 to 19, adapted to provide a method of treatment according to any one of claims 1 to 15.

15 21. A method by which the Threshold Plasma Concentration for a given anti diabetic compound can be determined by the steps:

20 1) first to obtain plasma concentrations versus time data for the compound by using standard pharmacokinetic compartmental modelling methods;

2) the model predicted concentrations for the compound are then fed back into the model and used to determine the change in fasting plasma glucose levels after various doses;

25 3) the relationship between predicted plasma concentrations of compound and fasting plasma glucose can then be determined using an indirect pharmacological response model.